NDA 21-071/S-006 8 FEB 2001

SmithKline Beecham
Attention: Sharon W. Shapowal, R.Ph.
Director, Avandia U.S. Regulatory Affairs
One Franklin Plaza - P.O. Box 7929
Philadelphia, PA 19101

Dear Ms. Shapowal:

Please refer to your supplemental new drug application dated May 26, 2000, received May 30, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Avandia® (rosiglitazone maleate) Tablets, 2 mg, 4 mg and 8 mg.

This supplemental new drug application initially proposed changes to the package insert in the **PRECAUTIONS** section, **Edema, Use in Patients with Heart Failure, Hepatic Effects,** and **Information for Patients** subsections. In the **PRECAUTIONS** section, **Hepatic Effects** subsection, specific addition of post-marketing safety information related to hepatic adverse events in association with Avandia use was proposed.

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the supplemental application is approved effective on the date of this letter. As discussed with you, this labeling change is to occur simultaneously with our **approvable** action on supplement 004. Supplement 004 proposed a new indication for the use of Avandia in combination with insulin in patients with Type 2 diabetes mellitus.

The labeling being approved with supplement 006 contains additional changes in several sections of the package insert. These changes include a new **CLINICAL STUDIES** section, a new **WARNINGS** section and **Cardiac Failure and Other Cardiac Effects** subsection, and revisions in the **PRECAUTIONS** section **Edema** and **Weight Gain** subsections, and in the **ADVERSE REACTIONS** section. These changes address safety issues related to the combined use of Avandia and insulin, arising from the review of supplement 004.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted February 8, 2001).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-071/S-006." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Ms. Jena Weber, Regulatory Project Manager, at (301) 827-6422.

Sincerely,

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research